

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Art Unit

Examiner:

Applicant:

Hovanes John Ter-Zakarian

Serial No:

Filed:

For:

FMF TREATMENT

-----  
Pasadena, California  
April 13, 2004


DISCLOSURE STATEMENT

Commissioner for Patents  
Alexandria, VA 22313-1450

Sir:

Examiner's attention is directed to the  
following patents: none

Respectfully submitted,

  
William W. Haefliger  
Attorney for Applicant  
Registration No. 17,120  
Area code 323 684-2707

WWH:hk  
Docket 12,616

TO WHOM IT MAY CONCERN:

5                   BE IT KNOWN THAT I, HOVANES JOHN TER-ZAKARIAN,  
a citizen of the United States of America, residing in  
Glendale, in the County of Los Angeles, State of  
California, have invented a new and useful improvement  
in

10  
  
FMF TREATMENT

## BACKGROUND OF THE INVENTION

5 This invention relates generally to  
improvements in treatment control primarily of the  
disease known s FMF (Familian Mediterranean Fever).

10 FMF is a widely known disease affecting  
millions of human beings, and there is consequently  
great need for effective treatment of humans suffering  
from FMF.

## SUMMARY OF THE INVENTION

15 It is a major object of the invention to  
provide effective treatment for FMF, including  
improvements in FMF control; and in this regard, it has  
now been discovered that effective control of FMF in  
humans is achieved by administering, on an average daily  
basis, between 5 and 15 milligrams of LTRA to a patient  
20 suffering from FMF.

Such administering of LTRA is preferably  
orally, such as in tablet form. As will be seen, it is  
preferred that about 10 milligrams of LTRA be  
administered, on an average daily basis, for at least as

long as significant FMF conditions are observed in a human being or patient, for example someone between 9 and 72 years of age. It has been discovered that FMF symptoms can thereby be eliminated.

5

#### DETAILED DESCRIPTION

As stated, it has been discovered that effective control of FMF in humans is achieved by oral administration of LTRA in the dosages referred to above. FMF is an inherited disorder usually characterized by recurrent episodes of fever and peritonitis (inflammation of the abdominal membrane).

Researchers have identified the gene of FMF and found several different gene mutations that cause this inherited rheumatic disease. The gene, found on chromosome 16, codes for a protein that is found particularly in granulocytes - which are white blood cells associated with the immune response. That protein is believed to assist in keeping inflammation under control by deactivating the immune response. Otherwise, a full-blown inflammatory reaction occurs; i.e. an attack of FMF.

FMF sufferers undergo bouts of fever,  
typically with severe abdominal pain associated with  
inflammation of the abdominal cavity (peritonitis).  
Attacks can also include arthritis, skin rashes, and  
5 chest pain from inflammation of the lung cavity.  
Certain patients develop amyloidosis, a potentially  
deadly accumulation of protein in vital organs such as  
the kidneys.

The only present treatment for FMF is a drug,  
10 known as colchicine, which patients need to take every  
day, for life, and which causes side effects such as  
diarrhea and abdominal cramps.

FMF occurs most commonly in people of non-  
Ashkenzi Jewish, Armenian, Arab and Turkish background  
15 living in the United States and abroad. As many as 1 in  
200 people in these populations have the disease, and as  
many as one in five to one in seven carry a mutated FMF  
gene. A person must inherit two mutated copies of the  
gene -- one from each parent -- in order to acquire FMF.

20 LTRA as referred to above is the acronym for  
leukotriene receptor antagonists, which block substances  
in the body known as leukotrienes. The latter are  
derived from the action of enzyme 5-lipoxygenase on

arachidonic acid, and are chemicals which cause asthma symptoms.

One synthetic LTRA is known as ZAFIRLUKAST with the chemical name of 4-5-cyclopentyloxy-carbonylamino-1-methyl-indol-3-ylmethyl-3-methoxy-N-o-tonylsulfanylbenzamide.

Another synthetic LTRA is known as SINGULAIR, a product of Merck & Co., Whitehouse Station, New Jersey. Montelukant sodium, the active ingredient in SINGULAIR, has the formula  $C_{35}H_{35}ClNNaO_3S$ .

The preferred method of improving FMF control in humans, or of treating FMF sufferers, includes administering on an average daily basis, between 5 and 15 milligrams of LTRA to a patient suffering from FMF. Such LTRA is preferably administrated orally, as in tablet form, and daily, for as long as FMF symptoms persist. Preferably about 10 milligrams of LTRA is administered, on a daily basis, to humans between 9 and 72 years of age. Such tablets may consists of the product known as ZAFIRLUCAST, or the Merck & Co., Inc. product known as SINGULAIR.

### TEST RESULTS

5           Over 20 patients were treated as described above, for periods of time varying from 5 months to 2 1/2 years, i.e. until FMF symptoms (fever, acute attacks, etc) were no longer detected, in all cases. LTRA dosages were approximately 10 milligrams daily, in tablet form.